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Attorney Docket No. P30835Div2C2

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE***7/ Declaration*

Applicant: Pathak et al.

May 8, 2002

Serial No.: 10/044,848

Group Art Unit No.: 1615

Filed: January 11, 2002

Examiner: A. Pulliam

For: FORMULATIONS, TABLETS OF PAROXETINE AND PROCESS TO PREPARE  
THEM**DECLARATION OF DR. DAVID GEORGE DOUGHTY**

I hereby declare and state that:

1. I am a co-inventor of the above-identified patent application;
2. I received my Ph.D. in Organic Chemistry from Teesside Polytechnic in 1977;
3. I belong to the following professional organizations:  
  
Fellow of the Royal Society of Chemistry; Chartered Chemist: Member 1977-Present.  
  
Member of the Institute of Operations Management, 1996-Present.
4. My major areas of research include:  
Product development  
Organic Chemistry  
Pharmaceutical process development and scale-up  
Technology transfer and  
Operations management.

I have published 5 articles and I am listed as an inventor on 4 patents relating to my efforts in the above research areas.

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5. I have been employed by SmithKline Beecham p.l.c., assignee of the above-identified patent application (and its predecessor company, Beecham Pharmaceuticals), now GlaxoSmithKline p.l.c., from 1977 to date. I am currently the Director of Process Innovation within the Pharmaceutical Development Department.
6. I have reviewed the exchange of official correspondence with the United States Patent and Trademark Office concerning the parent application (U.S. Application No. 09/411,764) of the above-identified application. In particular, I have reviewed the Office Actions dated July 12, 2001, and November 29, 2000, the response dated May 29, 2001, and the Examiner Interview Summary Record of January 10, 2002.
7. I understand the outstanding issues related to my patent application to be as follows:
  - (i) the Barnes patent (U.S. Patent No. 4,721,723) is cited against the subject matter of pending claims 16 and 17, which is the same subject matter as that claimed in claims 54 and 55 of the parent application;
  - (ii) the Examiner requests a declaration supporting that the tablets of claims 16 and 17 are patentably distinct from those of the prior art and that the differences are the result of the dry process described in claims 16 and 17; and
  - (iii) the Examiner requests that the declaration show that the unexpected results achieved by the claimed tablets occur irrespective of the excipient used.
8. I have the following comments regarding (i), (ii) and (iii) above.
  - (i) I have reviewed the patent to Barnes and pending claims 16 and 17. This patent is directed to a new crystalline form of paroxetine, a hemihydrate form. Column 5, lines 60 to 64 of Barnes mention that preferred unit dosage forms for the new form of paroxetine include, but presumably are not limited to, tablets or capsules. Further, lines 62 to 64 indicate that the compositions of Barnes may be formulated by conventional methods of admixture, such as blending, filling and compressing.

Pharmaceutical tablets can be prepared by numerous processes. For example, pharmaceutical tablets can be formulated by wet or dry methods, and both of these methods can be formulated by granulation or direct compression procedures. The suitability of each of these methods depends on the characteristics of the pharmaceutical agent. Each of these methods can impart different physical

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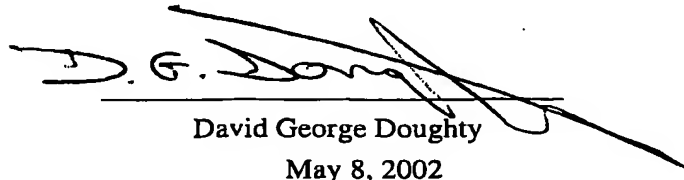
characteristics to the final tablet. Some of these characteristics may be favourable and some of these characteristics may be detrimental to the final tableted product of a given pharmaceutical agent. As one skilled in the art of pharmaceutical formulation, I understand the Barnes patent, and particularly Column 5, lines 60-64 thereof, to indicate that the new crystalline hemihydrate form of paroxetine can be formulated into various tablet and capsule preparations with acceptable results using conventional methods of admixture.

- (ii) As described in my patent application on page 1, lines 15 and 16, all marketed prior tablet formulations of paroxetine were formulated using an aqueous granulation process. On a commercial scale, this process produced unacceptable formulations in that a highly undesirable pink hue was intermittently formed on a batch to batch basis. See page 1, lines 20-21. The Barnes patent does not contain any examples of paroxetine formulations prepared by any process. My invention, as described in my patent application, is directed to the surprising discovery that the formulation of paroxetine into tablets can be carried out reliably and on a commercial scale using a formulation process in which water is absent.
- (iii) It is my experience and part of my discovery, as described in my patent application, that, in preparing commercial scale formulations containing paroxetine, formulations prepared in the absence of water are less likely to develop a pink hue. Further, it is my experience and part of my discovery that the reduction in the development of a pink hue and the discovery of a preferred process for commercial scale tablet production of paroxetine is related to the formulation being run in the absence of water, and not related to any particular blend of excipients. By way of example, a pharmaceutical formulation was prepared by admixing paroxetine with pregelatinized starch) as the excipient, and filling the mixture into capsule shells. No pink hue developed in the formulation after manufacture, or during stability testing.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.



David George Doughty  
May 8, 2002

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